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14. ABSTRACT

The ability to accurately and efficiently monitor the neurocognitive status of US warfighters under diverse operational and experimental conditions is of critical importance to the ongoing mission and Force 2025 objectives of the United States military. The Automated Neuropsychological Assessment Metrics (ANAM) is a computer assisted tool for evaluating neurocognitive performance with demonstrated effectiveness for application in diverse military operational and research testing scenarios. The primary objective of this project is to examine select psychometric and administration properties of the ANAM4. Four studies were proposed as part of this overall effort: 1) examine common use practices and determine the effect of specific administration procedures on ANAM4 performance, 2) assess the test-retest reliability of individual ANAM4 tests, 3) examine the validity of the ANAM4 mood scale and 4) establish a representative normative dataset of ANAM4 performance outcomes specifically for use with Army National Guard service members. Data collection for Studies 1-3 is complete; data collection for Study 4 is ongoing. Data analyses and manuscript preparation for all four studies is ongoing.

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ANAM, cognitive, assessment, psychometrics, validity, reliability, normative

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INTRODUCTION

The ability to accurately and efficiently monitor neurocognitive status of U.S. warfighters under diverse operational and experimental conditions is of critical importance to the ongoing mission and Force 2025 objectives of the U.S. military. The Automated Neuropsychological Assessment Metrics Version 4 (ANAM4) is a computer-assisted tool for evaluating neurocognitive performance with demonstrated efficacy for application in diverse military operational and research testing scenarios. The primary objective of this multi-study project is to examine select psychometric and administration properties of the ANAM4. This project includes four studies that address different psychometric and administrative elements of the ANAM4, each critical to the understanding and utilization of this automated cognitive testing system. Study 1 examines common use practices and their impact on ANAM4 performance. Study 2 assesses the test-retest reliability of individual ANAM4 test modules. Study 3 examines the validity of the ANAM4 mood scale. Study 4 will establish a representative normative dataset of ANAM4 performance outcomes specifically for Army National Guard Service members.

Body

This project (which includes four studies) was funded 01 December 2007. The approved study timeline/SOW is presented in **Table 1.**

Table 1: Statement of Work/Study Timeline (Original, 2007)

Year 1	**Months 1-2**	**Task 1**	Plan and finalize logistics for Phase I (Studies 1-3)
	Months 3-12 (Dec 2008)	**Task 2**	Subject recruitment, data collection and data management for Studies 1-3
Year 2	**Month 13-14**	**Task 3**	Perform preliminary data analyses for Study 3
	Month 15-24 (Dec 2009)	**Task 4**	Complete data collection for Study 1
		Task 5	Perform preliminary data analyses for Study 1
		Task 6	Continue recruitment, data collection and data management for Study 2 & 3
		Task 7	Complete data collection for Study 3
Year 3	**Month 25-36 (Dec 2010)**	**Task 8**	Complete data collection for Study 2
		Task 9	Plan and finalize logistics for Phase II (modified Study 4)
		Task 10	Complete data analyses for Studies 1, 2, 3
		Task 11	Preparation of journal manuscript(s) for Studies 1, 2, 3
		Task 12	Preparation of Project report for Studies 1, 2, 3
		Task 13	Set-up data management procedures for Study 4
Year 4	**Month 37-48 (Dec 2011)**	**Task 14**	Initiate data collection procedures for Study 4
		Task 15	Carry out data collection procedures for Study 4
		Task 16	Initiate integrative data management structure set up for Study 4
		Task 17	Operationalize database for Study 4 analysis scheme
		Task 18	Perform preliminary data analyses for Study 4
		Task 19	Complete data collection procedures for Study 4
Year 5	**Month 49-60 (Dec 2012)**	**Task 20**	Complete data analyses for Study 4
		Task 21	Prepare Study 4 manuscript(s) for peer review
		Task 22	Preparation of Project Final Report

A request for a 12 month no-cost extension for this study was approved on 7 November 2012, extending study activities through December 2013. A modified statement of work, approved as part of the no-cost extension, is presented in **Table 6**.

Table 6: MODIFIED SOW for remaining PROJECT Tasks and STUDY TIMETABLE (Nov 2012)

Year 4	**Month 37-48 (ending Dec 2011)**	**Task 14**	Initiate data collection procedures for Study 4
		Task 15	Carry out data collection procedures for Study 4
		Task 16	Initiate integrative data management structure set up for Study 4
		Task 17	Operationalize database for Study 4 analysis scheme
Year 5	**Month 49-60 (ending Dec 2012)**	**Task 18**	Conduct data collection procedures for Study 4 (contôd)
		Task 19	Complete manuscript preparations/submissions for Studies 1-3
		Task 20	Set up/operationalize data analyses plan for Study 4
Year 6	**Month 61-72 (ending Dec 2013)**	**Task 21**	Complete data collection for Study 4
		Task 22	Complete data analyses for Study 4
		Task 23	Prepare Study 4 manuscript(s) for peer review
		Task 24	Preparation of Project Final Report

A request for an additional 12 month no-cost extension for this study was approved on 25 September 2013, extending study activities through December 2014. The modified statement of work is presented in **Table 7**.

Table 7. MODIFIED SOW for remaining PROJECT Tasks and STUDY TIMETABLE (Nov 2013)

Year 5	**Month 49-60 (ending Dec 2012)**	**Task 18**	Conduct data collection procedures for Study 4 (contôd)
		Task 19	Continue manuscript preparations/submissions for Studies 1-3
		Task 20	Set up/operationalize data analyses plan for Study 4
Year 6	**Month 61-72 (ending Dec 2013)**	**Task 21**	Continue data collection for Study 4
		Task 22	Continue manuscript preparations/submissions for Studies 1-3
Year 7	Month 73-84 (ending Dec 2014)	**Task 23**	Complete data collection for Study 4
		Task 24	Complete data analyses for Study 4
		Task 25	Complete manuscript preparations/submissions for Studies 1-3
		Task 26	Prepare Study 4 manuscript(s) for peer review
		Task 27	Preparation of Project Final Report

A request for a final 12 month no-cost extension for this study was approved on 28 October 2014, extending study activities through November 2015. The modified statement of work is presented in **Table 8**.

Table 8. MODIFIED SOW for remaining PROJECT Tasks and STUDY TIMETABLE (Oct 2014)

Year 5	**Month 49-60 (ending Dec 2012)**	**Task 18**	Conduct data collection procedures for Study 4 (contôd)
		Task 19	Complete manuscript preparations/submissions for Studies 1-3
		Task 20	Set up/operationalize data analyses plan for Study 4
Year 6	**Month 61-72 (ending Dec 2013)**	**Task 21**	Conduct data collection for Study 4 (contôd)
		Task 22	Initiate data quality control checks and preliminary analyses for Study 4
Year 7	**Month 73-84 (ending Dec 2014)**	**Task 23**	Initiate external data request procedures for Study 4
		Task 24	Conduct data collection procedures for Study 4 (contôd)
		Task 25	Continue data quality control checks and preliminary analyses for Study 4 Following each data collection trip, the newly collected data are entered into database and cleaned and preliminary data checks conducted
		Task 26	Complete 100% data collection goal for Study 4 (with ARNG national sample from at least 8 geographically representative US states)
Year 8	**Month 85-96 (ending Dec 2015)**	**Task 27**	Complete data analyses for Study 4 • With 100% data collected, complete data analyses to address Study 4 research hypotheses
		Task 28	Prepare Study 4 manuscript(s) for peer review • With completion of Study 4 analyses and manuscript preparation, travel to present findings at national conference forum is planned
		Task 29	Preparation of Project Final Report

<u>Task 1 (Month 1-2)</u>
Plan and finalize logistics for Phase I (Studies 1-3) – COMPLETED
All logistical aspects for HURC approved studies (Studies 1-3) have been confirmed. Recruitment procedures, equipment, testing facilities, and other data collection elements have been finalized and are now complete

<u>Task 2 (Month 3-12)</u> Subject recruitment logistics, data collection and data management for Studies 1-3 – COMPLETED
Subject recruitment, data collection and data management efforts have been completed for Studies 1-3. Recruitment of both Human Research Volunteers and Civilians was effective and efficient.

Task 3 (Month 15-24) Perform preliminary data analyses for Study 3– COMPLETED
All preliminary data analyses for Study 3 have been completed. Initial analyses suggested that additional participants would be necessary to explore noted differences between military and civilian participants on discrete on mood measures. Thus an amendment (#4, 14 July 2009) to increase enrollment from 50 to 80 participants was submitted and approved. Higher-level analyses are nearing completion on this expanded sample.

Task 4 (Month 15-24) Complete data collection for Study 1– COMPLETED
Study 1 involves the examination of common use practices and specific administration procedures (individual or group administration, practice or no practice, single session or two sessions) on ANAM4 task performances. Our recruitment goal for Study 1 was 90 participants, 30 participants per condition. Enrollment data are presented in **Table 2**.

Table 2. Study 1 Enrollment

# Participants Enrolled	90
# Participants Completed	86*

**NOTE: 15 participants completed the ANAM4 without practice test modules; 15 participants completed the ANAM4 in a group setting and 15 participants completed the ANAM4 in two administration sessions. The remaining 41 participants served as controls for these discrete administration scenarios (individual administration using practice test modules and completed in a single testing session). Thus each condition had at least 30 participants, as required.*

Task 5 (Month 15-24) Perform preliminary data analyses for Study 1 – COMPLETED
Preliminary analyses (sample characterization and demographic analyses) on the Study 1 data set have been completed.

Task 6 (Months 15-24) Subject recruitment, data collection and data management for Studies 2 & 3 – COMPLETED
Our recruitment goal for Study 2 was 90 participants, 30 participants per condition (days 1 & 7 / days 1 & 30 / 7 consecutive day retest). Recruitment goal for Study 3 was 80 participants. Recruitment goals were reached for Studies 2 and 3 and data collection has been completed for these studies.

Task 7 (Months 15-24) Complete data collection for Study 3 – COMPLETED
Data collection for Study 3 is complete. Enrollment data are presented in **Table 3**.

Table 3. Study 3 Enrollment

# Participants Enrolled	113
# Participants Completed	77

Task 8 (Months 25-36) Complete data collection for Study 2- COMPLETED
Data collection for Study 2 is complete. Enrollment data are presented in **Table 4**.

Table 4. Study 2 Enrollment

# Participants Enrolled	99
# Participants Completed	92

Task 9 (Months 25-36) Plan and finalize logistics for Phase II (modified Study 4) – COMPLETED

The Study 4 protocol has been reviewed and approved by USARIEM HURC and HRPO (final approval to initiate received June 2011). Endorsement of the study by the National Guard Bureau (NGB) was received 20 October 2011 and all 8 states (Arizona, Kentucky, Maine, Minnesota, Mississippi, Montana, Oklahoma, Pennsylvania) have been contacted by both NGB and study staff. Oklahoma declined participation in September 2012. We identified Texas as a suitable replacement for Oklahoma and secured NGB endorsement for the state in October 2012.

Task 10 (Months 25-36) Complete data analyses for Studies 1, 2, 3 - IN PROGRESS

Preliminary data analyses have been completed for each of the studies. We continue to conduct higher-level analyses of these data, including new composite and effort analyses, within each of these studies.

Task 11 (Months 25-36) Preparation of journal manuscript(s) for Studies 1, 2, 3 – COMPLETED

Manuscripts for these studies have been drafted/prepared.

Task 12 (Months 25-36) Preparation of project report for Studies 1, 2, 3 – COMPLETED

Project summaries and completion of Studies 1-3 were included in previous continuing review reports. Manuscripts for these studies are in progress.

Task 13 (Months 25-36) Set-up data management procedures for Study 4 - COMPLETED

All procedures involving data management have been established. Study datasets have been created and are being populated as data are obtained from field sites. Data entry and checking have been successfully coordinated.

Task 14 (Months 25-36) Initiate data collection procedures for Study 4 – COMPLETED

Data collection procedures were initiated in Arizona, Montana and Maine in the prior reporting period (2012). Planning activities for data collection trips to Minnesota and Kentucky were initiated during this reporting period, with initial data collection trips completed in August (MN) and October (KY) of this period, respectively.

Task 15 (Months 37-48) Carry out data collection procedures for Study 4 – COMPLETED (See Task 18, 21, & 24 for further updates)

Data collection has been completed in three states: Arizona, Maine, and Montana.

Task 16 (Months 37-48) Initiate integrative data management structure set up for Study 4 - COMPLETED

Databases associated with Study 4 have been created and are being populated as data are obtained and cleaned.

<u>Task 17 (Months 37-48)</u> Operationalize database for Study 4 analysis scheme – COMPLETED
Data entry has commenced and databases continue to be refined for analytic schemes.

<u>Task 18 (Months 49-60)</u> Conduct data collection procedures for Study 4 (cont'd) – CARRIED OUT (See Task 21 & 24 for further updates)
Data collection procedures were completed previously in three states (AZ, ME, MT) and have been initiated in three states (KY, MN, TX). Coordination of TAG-level approvals has been initiated with three states (Pennsylvania, Florida and Tennessee).

<u>Task 19 (Months 49-60)</u> Complete manuscript preparations/submissions for Studies 1-3- IN PROGRESS
We have completed primary data analyses for Studies 1-3 and manuscript preparations. Completion of higher-level analyses to finalize and submit to peer-reviewed journals is in progress.

<u>Task 20 (Months 49-60)</u> Set up/operationalize data analyses plan for Study 4 **– COMPLETED**
Operationalizing of the primary data analytic plan for Study 4 was set-up and completed.

<u>Tasks 21 (Months 61-72)</u> Conduct data collection for Study 4 (cont'd)– CARRIED OUT
Data collection is ongoing in three states (KY, MN, TX) and is being coordinated in a fourth state (NH). We are currently coordinating TAG-level approvals with three states (Pennsylvania, Florida, Tennessee). **(See Task 24 for current update)**

<u>Task 22 (Months 61-72)</u> Initiate data quality control checks and preliminary analyses for Study 4 - CARRIED OUT
Data quality control checks have been initiated and are ongoing as we complete each data collection trip.

<u>Task 23 (Months 73-84)</u> Initiate external data request procedures for Study 4 – CARRIED OUT
The external data request (with DMDC for military service history, AFQT, and additional demographic data) was initiated and completed for those participants from the three states in which data collection activities have been completed (AZ, MT, ME). A subsequent external data request will be made when data collection efforts with the remaining states are completed.

<u>Task 24 (Months 73-84)</u> Conduct data collection procedures for Study 4 (cont'd) – IN PROGRESS

Data collection is ongoing in with ARNG in three states (KY, MN, TX) and is being coordinated in a fourth state (NH). We are currently coordinating TAG-level approvals with three states (Pennsylvania, Florida, Tennessee). Coordination for additional data collection trips is ongoing.

In Minnesota, 62 % of the target sample (300) has been completed. Data collection also continues in Kentucky, with one trip conducted (July 2014) during the current reporting period and approximately 64% of the target sample (300) for this state completed. Data collection was initiated in Texas during this reporting period. Three trips were conducted in August, September and December of 2014, resulting in completion of 59% of the target sample for the state (300). New Hampshire was added as an approved study site in February 2014; coordination for data collection in this state in ongoing.

Current enrollment by state is presented in **Table 5**.

Table 5: Current Study 4 enrollment

State	# Completed
Arizona	223
Maine	250
Montana	301
Minnesota	185
Kentucky	193
Texas	177
Total	**1329**

Task 25 (Months 73-84) Continue data quality control checks and preliminary analyses for Study 4: Following each data collection trip, the newly collected data are entered into database and cleaned and preliminary data checks conducted – IN PROGRESS
Data quality control checks are ongoing. Preliminary analyses have been performed on data from the three states in which data collection has been completed (AZ, MT, ME) and were submitted as abstracts to professional conferences (See Appendix A and B for Abstracts).

Task 26 (Months 73-84) Complete 100% data collection goal for Study 4 (with ARNG national sample from at least 8 geographically representative US states) – IN PROGRESS

Task 27 (Months 85-96) Complete data analyses for Study 4: With 100% data collected, complete data analyses to address Study 4 research hypotheses - PENDING

Task 28 (Months 85-96) Prepare Study 4 manuscript(s) for peer review: With completion of Study 4 analyses and manuscript preparation, travel to present findings at national conference forum is planned – PENDING

Task 29 (Months 85-96) Preparation of Project Final Report - PENDING

KEY RESEARCH ACCOMPLISHMENTS

Key research accomplishments during the current study period include:

- Progress on Study 4 data collection was delayed due to a local (institute-level), administrative audit (April-June: 2.5 months) and cancellation of drill activities nationwide this past Fall as a result of funding issues.

- Data analyses, particularly higher-order analyses, continue for Studies 1 -3; manuscripts are in final preparation stages for Studies 1-3.

- Continuing Review report was reviewed and approved by the USARIEM IRB (15 August 2014) and the Army HRPO (23 September 2014).

- As described above, seven states have agreed to participate in Study 4 data collection and provided TAG-level approval; approvals are pending in three additional states.
    - During this reporting period, data collection activities were carried out in 2 states (KY, TX); in both states data collection is more than 50% completed
    - TAG-level approval was secured for NH and data collection coordination activates are underway.
    - We have been in active communication with three states (PA, FL, TN), all of which have indicated interest in the study; approvals are pending

- A 12 month no-cost extension for this study was approved on 28 October 2014, extending study activities through November 2015.

REPORTABLE OUTCOMES

Reportable outcomes during the current study period include:

1. Reports, manuscripts, abstracts (included in Appendix)

Proctor, S.P., Heaton, K.J., Dillon, C., Rudov, S., & Vincent, A.S. (2014). Descriptive Analyses of ANAM4 TBI Performance Among a National Sample of U.S. Army National Guard Soldiers. Poster presented at the Annual Meeting of the Association of Military Surgeons of the United States. Washington, DC, Dec. 2, 2014.

Dillon, C., Proctor, S.P., Vincent, A.S., & Heaton, K.J. (abstract submitted). Demographic differences on ANAM4 TBI performance among US Army National Guard Soldiers. Submitted for Poster Presentation at the 123rd Annual Convention of the American Psychological Association, Toronto, Ontario, Canada, August 2015.

2. Degrees and research training opportunities

In addition to Drs. Proctor and Heaton, one doctoral-level researcher, three pre-doctoral interns, five masters-level interns, and three bachelorôs-level research assistants are currently trained to administer the Study 4 protocol for this project.

During the current reporting period, 5 research assistants affiliated with this project applied to and were accepted into doctoral/medical programs.

3. Collaborative funding applications related to work supported by this award

- ñEye-Tracking Rapid Attention Computation (EYE-TRAC)ò (USARIEM Protocol # H09-07; Site PI: Heaton). This project was funded as a FY08 CDMRP Advanced Technology Award to Dr. Jamshid Ghajar, Brain Trauma Foundation, New York, NY (W81XWH-08-2-0646). This study examines the efficacy of a novel visual tracking system for assessing the integrity of the attention system. The ANAM4-TBI-MIL battery was used in this study to provide cognitive performance outcomes for validation of the visual tracking paradigm. Healthy military volunteers were subjected to a 26-hour period of sleep loss during which cognitive and visual tracking performance were evaluated. Test-retest reliability of the ANAM4-TBI-MIL was examined across a 2 week interval and sensitivity of the ANAM4 TBI battery to central fatigue were determined. Two papers (one published, the other pending) and one abstract (submitted) involve ANAM4-TBI-MIL data collected from this study:

  Heaton KJ, Maule AL, Maruta J, Kryskow EM, Ghajar J. Attention and Visual Tracking Degradation During Acute Sleep Deprivation in a Military Sample. *Aviation, Space, and Environmental Medicine.* May 2014; 85(5):497-503. DOI: 10.3357/ASEM.3882.2014.

  Heaton, K.J., Laufer, A.S., Maule, A., Vincent, A.S. Effects of acute sleep deprivation on ANAM4 TBI Battery performance in healthy US Army Service Members. *In preparation*

  Heaton, K.J., Laufer, A.S., Maule, A., Vincent, A.S. (abstract submitted). Effects of acute sleep deprivation on ANAM4 TBI Battery performance in healthy US Army Service Members. Submitted for Poster Presentation at the 123rd Annual Convention of the American Psychological Association, Toronto, Ontario, Canada, August 2015.

- ñAn Investigation of the Effects of Head Impacts Sustained during Collegiate Boxing Participation on Central and Peripheral Nervous System Functionò (USAFA Protocol # FAC2007010H, PI: MAJ Brandon Doan, USAFA), was funded in part by an AMEDD Advanced Medical Technology Initiative (AAMTI) award to Dr. Heaton. In this study,

the effects of mild, repetitive head impacts sustained during amateur boxing training bouts on cognitive performance outcomes were examined using the ANAM4-TBI-MIL and IMPACT cognitive test batteries. One manuscript has been submitted for review related to this work:

Heaton KJ, Adam GE, Butler MA, Self B, Brininger T, Wile A, Rudolph KA, Doan B. Mild Repetitive Head Impacts and Neurocognitive Performance in Amateur Military Boxers. Submitted to British Journal of Sports Medicine. *Under review*

- ñIdentifying biomarkers that distinguish post-traumatic stress disorder and mild traumatic brain injury using advanced magnetic resonance spectroscopy,ò was funded via a Department of Defense Congressionally Directed Medical Research Programs Psychological Health/Traumatic Brain Injury (PH/TBI) Research Program award to Dr. Alex Lin, Brigham and Womenôs Hospital, Boston, MA. Dr. Heaton is a co-Investigator and site PI on this project. This study proposes a multi-parametric approach using major advances on spectroscopic methods and neuroimaging to identify biomarkers that can be used to distinguish between post-traumatic stress disorder, traumatic brain injury, and their co-occurrence. This will be achieved in part by correlating quantitative MR spectroscopy results with behavioral and neuropsychological metrics (including ANAM4TBI) using newly developed algorithmic approaches that are capable of revealing discriminating metabolic markers in MR spectroscopy measurements. Data collection for this project is ongoing.
- ñMultimodal Assessment of Cognitive Readiness and Recovery: Initial Modeling of Physiological and Neurological Inputsò (USARIEM Protocol 15-05HC; PI: Heaton), was funded by Defense Health Program (DHPe, RDT&E, Operational Performance Sustainment; ñMultimodal Assessment of Cognitive Readiness and Recovery: Modeling and Analysis of Physiological and Neurological Inputsò) to Dr. Heaton and MIT Lincoln Laboratory investigator, Dr. Thomas Quatieri. This study will examine the sensitivity of a multi-modal platform for detecting change in cognitive functioning under different cognitive load conditions. The platform consists of vocal, facial, physiological (heart rate, skin conductance, respiration), and cognitive data inputs. The ANAM4 is included in the cognitive test battery. This protocol is currently under review.

4. Related projects and collaborations initiated

- ñAnalyses of ANAM4Ê TBI Predeployment Assessment Data: USARIEM-OTSG Research Collaborativeò (USARIEM #11-07HC; PI: Proctor)involves the creation of a research database system (ANAM4TBI Military Performance Database (AMP-D)) which incorporates all mandated pre-deployment ANAM4TBI assessment data from DoD military personnel (maintained by the Office of the Surgeon General, ANAM Program Office). We have initiated the process of linking these neurocognitive data with individual military service, demographic, and injury and clinical disease histories. At the conclusion of Study 4, we plan utilize the AMP-D to make comparisons between Army

Active Duty and National Guard groups and examine the role of deployment-related factors on neurocognitive health and performance. A manuscript detailing the AMP-D and population demographics was submitted and has been accepted for publication:

> Proctor, S.P., Nieto, K., Heaton, K.J., Dillon, C.C., Schlegel, R.E., Russell, M.L., & Vincent, A.S. (*in press*). Neurocognitive Performance and Prior Injury among U.S. Department of Defense Military Personnel Military Medicine.

- ñValidation of Select Neurobehavioral Assessments for Concussion/Mild Traumatic Brain Injury (MTBI)ò (USARIEM #H09-08), was intramurally funded (MRMC RAD3) to Drs. Proctor and Heaton (co-PIs). This study seeks to validate the ANAM4TBI Battery against a standard neuropsychological screening battery for mild traumatic brain injury. The project is nearing completion.

- ñMultidimensional MR Imaging to Assess Subtle Brain Changes Associated with Persistent Postconcussive Symptoms (PPCS) Following Mild Traumatic Brain Injuryò (USARIEM Protocol #11-15-HC; PI: Palumbo, co-I: Heaton), was intramurally funded (MRMC RAD3) to Dr. Palumbo (co-I: Heaton). This study examines neuropathological changes associated with PPCS following mTBI using multidimensional magnetic resonance imaging (MRI) to determine the independent and synergistic effects of structure, function, connectivity and blood flow of the brain in subjects with mTBI. ANAM4-TBI-MIL is being used in this study to examine cognitive performance outcomes. Data collection for this study is ongoing.

CONCLUSION

Analyses of data from Studies 1-3 will be completed, and reported in the coming (final) review period. Our results (reported in conference proceedings included in the 2010 Annual Report for this project) provide evidence supporting the Automated Neuropsychological Assessment Metrics Version 4 (ANAM4) as a reliable and valid measure of cognitive performance under diverse administration scenarios.

Results from Study 4 are currently pending completion of data collection involving development of a nationally-representative normative dataset of Army National Guard service membersô ANAM4 performance outcomes. This dataset is intended to complement existing normative data by focusing on a subset of the general military population that research has shown differs on key demographic elements (e.g., dual career status, average age, marital and family status, and education)) relative to other military components (e.g., Active Duty), and as such, is expected to facilitate the interpretation of individual National Guard service membersôperformance on ANAM4 tests.

Together, results from all four studies in this project will add to ongoing efforts to develop and validate the ANAM4 as an accurate, reliable and objective measure of military service membersô cognitive performance.

APPENDIX

Appendix A: Proctor, S.P., Heaton, K.J., Dillon, C., Rudov, S., & Vincent, A.S. (2014). Descriptive Analyses of ANAM4 TBI Performance Among a National Sample of U.S. Army National Guard Soldiers. Poster presented at the Annual Meeting of the Association of Military Surgeons of the United States. Washington, DC, Dec. 2, 2014.

Appendix B: Dillon, C., Proctor, S.P., Vincent, A.S., & Heaton, K.J. (abstract submitted). Demographic differences on ANAM4 TBI performance among US Army National Guard Soldiers. Submitted for Poster Presentation at the 123rd Annual Convention of the American Psychological Association, Toronto, Ontario, Canada, August 2015.

Appendix C: Heaton, K.J., Laufer, A.S., Maule, A., Vincent, A.S. (abstract submitted). Effects of acute sleep deprivation on ANAM4 TBI Battery performance in healthy US Army Service Members. Submitted for Poster Presentation at the 123rd Annual Convention of the American Psychological Association, Toronto, Ontario, Canada, August 2015.

Appendix D: Heaton KJ, Maule AL, Maruta J, Kryskow EM, Ghajar J. Attention and Visual Tracking Degradation During Acute Sleep Deprivation in a Military Sample. *Aviation, Space, and Environmental Medicine.* May 2014; 85(5):497-503. DOI: 10.3357/ASEM.3882.2014.

APPENDIX A

Proctor, S.P., Heaton, K.J., Dillon, C., Rudov, S., & Vincent, A.S. (2014). Descriptive Analyses of ANAM4 TBI Performance Among a National Sample of U.S. Army National Guard Soldiers. Poster presented at the Annual Meeting of the Association of Military Surgeons of the United States. Washington, DC, Dec. 2, 2014.

ABSTRACT

Limited research has focused on the neurological health and performance of U.S. Army National Guard (ARNG) personnel. In light of the dual-job occupational histories and demographic differences (i.e., older, more years of education) of ARNG compared to their Active Duty (AD) counterparts, it is important to identify and characterize possible performance differences on measures of cognitive function.

Current efforts are underway to develop a national reference sample of ARNG Soldiersô performance on the Automated Neuropsychological Assessment Metrics (version 4) TBI Military (ANAM4 TBI-MIL) battery. This reference sample will be comprised of data from a representative sample of 2,400 ARNG Soldiers from 8-10 U.S. states.

Descriptive analyses of questionnaire and performance data (n=695) from three states completed to date (Montana, Maine, and Arizona) were performed. The ARNG sample was 15% female and 30.6 (SD=9.1) years old on average; the majority (64%) had completed education beyond the high school level. ANAM4 TBI-MIL task performance was compared to published normative data from AD personnel (10% female and mean age 27.4 (SD=7.4) years). Overall, no significant performance differences were observed between the ARNG and AD on tasks involving visual memory and complex attention, while ARNG personnel performed with significantly reduced efficiency ($p<.001$) on tasks of simple attention and psychomotor speed. When comparative analyses were restricted to those 21-25 years of age, no significant differences in performance were observed.

In conclusion, neurocognitive performance differences between AD and ARNG were observed on certain neurocognitive tasks, however, results suggest these are related to demographic factors (i.e., age).

DISCLAIMER: The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Army.

APPENDIX B

Dillon, C., Proctor, S.P., Vincent, A.S., & Heaton, K.J. (abstract submitted). Demographic differences on ANAM4 TBI performance among US Army National Guard Soldiers. Submitted for Poster Presentation at the 123rd Annual Convention of the American Psychological Association, Toronto, Ontario, Canada, August 2015.

ABSTRACT

Several studies have examined the neurocognitive performance of the U.S. military, particularly Active Duty personnel. However, minimal research has focused on the neurocognitive performance of U.S. Army National Guard (ARNG) Soldiers. Known demographic differences between Active Duty and Reserve/National Guard personnel on such factors as age and education level may influence neurocognitive proficiencies. Thus, the goal of this analytic study was to examine the role of demographic factors on neurocognitive test performance within a multi-state cohort of ARNG personnel.

The Automated Neuropsychological Assessment Metrics (version 4) TBI Military (ANAM4 TBI-MIL) battery was developed to assess general cognitive functioning, specifically following injuries to the head. A normative dataset for the ANAM4 TBI-MIL has been created for use with U.S. Active Duty personnel. Comparable reference data are not currently available for use with Army National Guard personnel specifically. Use of appropriate reference data is critical to the accurate interpretation of test performance. Data collection from a sample of ARNG personnel designed to be representative of the current U. S. ARNG population is ongoing and upon completion will include ANAM4 TBI-MIL performance data from approximately 2,400 ARNG Soldiers from 8-10 U.S. states.

Performance data were analyzed from three states completed to date (Arizona, Maine, and Montana; n=695). The ARNG sample was 15% female and 30.6 (SD=9.1) years old on average; the majority (64%) had completed some education beyond the high school level. Significant performance differences were observed between age groups (18-24 years old; 25-34 years old; 35 years and older), with younger participants performing better on tasks measuring sustained attention, reaction time, processing efficiency, visuospatial working memory and delayed memory ($p<.001$). There was a significant benefit of advanced education (high school or equivalent vs. greater than high school) on a one test measuring basic computational skills and processing speed ($p<.001$). This benefit is not associated or confounded by age. There were no observed differences in task performance between male and female participants.

In conclusion, neurocognitive performance differences on the ANAM4 TBI-MIL battery were associated with age. However, minimal to no performance differences related to education and gender were observed. Further evaluation of demographic factors will be conducted with the complete multi-state cohort of ARNG personnel.

APPENDIX C

Heaton, K.J., Laufer, A.S., Maule, A., Vincent, A.S. (abstract submitted). Effects of acute sleep deprivation on ANAM4 TBI Battery performance in healthy US Army Service Members. Submitted for Poster Presentation at the 123rd Annual Convention of the American Psychological Association, Toronto, Ontario, Canada, August 2015.

Introduction: The Automated Neuropsychological Assessment Metrics (version 4) Traumatic Brain Injury Battery for the Military (ANAM4 TBI-MIL) is currently being used within the U.S. Army as part of a comprehensive brain injury/concussion screening program, providing a broad measure of cognitive function to aid clinicians in the assessment and treatment of brain injuries. Numerous factors endemic to military operational and training environments, including physical and mental fatigue, have been shown to produce shifts in cognitive status and mood in prior research involving military and civilian populations. Thus, the presence of these factors may confound the interpretation of cognitive performance. Although the effects of sleep loss on cognitive function have been examined in earlier versions of the ANAM, the impact of sleep loss on ANAM4 TBI-MIL battery performance outcomes has not yet been reported. Understanding the influence of factors such as fatigue on ANAM4 TBI-MIL performance is critical for accurate interpretation of test results in military service members. The impact of fatigue is also an important component of injury prevention and ensuring optimal performance and mission readiness of military service members.

Methods: The effects of acute (26 hours)sleep deprivation on cognitive performance as evaluated by the ANAM4 TBI-MIL battery were examined in 87 healthy US Army service members (68 men, 19 women), ranging in age from 18-33 with an average of 12.5 years of education. The ANAM TBI-MIL battery consists of a sleepiness scale, a mood scale and 7 additional test modules assessing reaction time, memory, processing efficiency, working memory, basic computational skills and attention. Participants completed the ANAM4 TBI-MIL battery three times during the sleep deprivation period: initial waking (baseline), ~20 hours awake, and ~26 hours awake.

Results: Across the 26 hour period of sleep loss, participants demonstrated increasingly slowed response times on 5 of the 7 cognitive test modules, including tasks of simple response speed, visual memory, working memory, processing efficiency and attention (p-values ranging from .014 to < .000). Degraded accuracy was observed on 3 of the 7 cognitive test modules, including working memory, processing efficiency, and visual memory tasks) (p-values < .000). In addition, participants reported an increase in sleepiness, a decrease in vigor and happiness and increased levels of restlessness, anxiety, anger/irritability and depressed affect (p values ranging from .002 to < .000).

Conclusions: Consistent with prior research involving ANAM and other cognitive assessment tools, results show degraded response speed and accuracy across most test modules of the ANAM4 TBI-MIL battery following a period of acute sleep deprivation. These findings provide evidence of the sensitivity of the ANAM4 TBI-MIL battery to the effects of acute sleep deprivation, an important consideration when evaluating service members in operational settings.

The views expressed in this presentation are those of the authors and do not reflect the official policy of the Department of the Army or the Department of Defense.

APPENDIX D

Attention and Visual Tracking Degradation During Acute Sleep Deprivation in a Military Sample

Kristin J. Heaton, Alexis L. Maule, Jun Maruta, Elisabeth M. Kryskow, and Jamshid Ghajar

Heaton KJ, Maule AL, Maruta J, Kryskow EM, Ghajar J. ***Attention and visual tracking degradation during acute sleep deprivation in a military sample.*** **Aviat Space Environ Med 2014; 85:497–503.**

Background: Fatigue due to sleep restriction places individuals at elevated risk for accidents, degraded health, and impaired physical and mental performance. Early detection of fatigue-related performance decrements is an important component of injury prevention and can help to ensure optimal performance and mission readiness. This study used a predictive visual tracking task and a computer-based measure of attention to characterize fatigue-related attention decrements in healthy Army personnel during acute sleep deprivation. ***Methods:*** Serving as subjects in this laboratory-based study were 87 male and female service members between the ages of 18 and 50 with no history of brain injury with loss of consciousness, substance abuse, or significant psychiatric or neurologic diagnoses. Subjects underwent 26 h of sleep deprivation, during which eye movement measures from a continuous circular visual tracking task and attention measures (reaction time, accuracy) from the Attention Network Test (ANT) were collected at baseline, 20 h awake, and between 24 to 26 h awake. ***Results:*** Increases in the variability of gaze positional errors (46–47%), as well as reaction time-based ANT measures (9–65%), were observed across 26 h of sleep deprivation. Accuracy of ANT responses declined across this same period (11%). ***Discussion:*** Performance measures of predictive visual tracking accurately reflect impaired attention due to acute sleep deprivation and provide a promising approach for assessing readiness in personnel serving in diverse occupational areas, including flight and ground support crews.

Keywords: arousal, oculomotor, smooth pursuit, validity, sleepiness.

MILITARY SERVICE members are frequently exposed to conditions that may contribute to disrupted sleep patterns. These conditions, which are often exacerbated during deployment, include extreme physical exertion, psychological or emotional stress, unpredictable or irregular work shifts, and extended mission durations. Within the aviation community, the link between fatigue and accident risk has long been established (1). Flight crews involved in long-haul missions (10) as well as those conducting short-haul operations (e.g., the low-cost air travel industry), where scheduling can be irregular and use of discretionary time for flight is commonplace (13), are at increased risk of fatigue-related accidents. Since the National Transportation Safety Board (NTSB) first cited fatigue as a probable cause in an aviation accident in 1993 (22), numerous fatigue-related accidents have been identified, including a Colgan Air accident in 2009 with 50 fatalities and an Air India crash in 2010 with 158 fatalities. It is estimated that nearly 15–20% of all aviation accidents are fatigue-related, involving flight and ground support crews (e.g., air traffic controllers, maintenance personnel, and fuel handlers) (1). Testimonies to the United States House of Representatives Subcommittee on Aviation by the National Aeronautical and Space Administration (NASA), the NTSB, and the Federal Aviation Administration regarding pilot fatigue and accident risk (8,21) underscore the importance of identifying and mitigating the effects of fatigue in flight crews and ground support personnel.

The impact of fatigue due to sleep loss on an individual's health and performance can be profound. Sleep loss or restriction increases risk of accidents and injury (24), alters immune function and elevates risk for illness (15), and impairs cognition, including executive function (18,23), decision making (14), attention (17,18,21), working memory (5), and visuospatial perception (14). Attention appears to be especially sensitive to sleep loss, even in the acute phase (17,18,21), but the precise characterization of attention degradation is challenging. Rather than a unitary function, attention has been described as a multidimensional system consisting of distinct but interacting neural networks (25). In particular, one theory posits three distinct but interrelated attention constructs. These include an alerting component (vigilance, achieving and maintaining activation of cognitive activity), an orienting component (allocating attentional focus selectively to relevant elements in the sensory environment), and an executive control/conflict component (maintaining control over one's behavior to achieve an intended goal and resolve conflict among competing alternative responses) (25). Research examining the effects of acute sleep deprivation have consistently shown reduced vigilance (alerting function) as measured by slower reaction times across a variety of tests (4,32), as well as impaired executive system function such as in decision making, response inhibition,

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planning, and error detection (14,23,31). These findings are supported by studies showing reductions in cerebral blood flow following a 26-h period of sustained wakefulness in regions related to alertness and attention, as well as other cognitive processes, particularly in the ventral regions of the prefrontal cortex and in the thalamus (5,30). Relatively few studies have examined the impact of sleep deprivation on the orienting function, and those that have report inconsistent results (4,33).

Early identification of fatigue-related performance decrements is an important component of injury prevention and can help to ensure optimal performance and mission readiness. However, measures that have demonstrated sensitivity to attention impairments following sleep loss/restriction may not differentiate the underlying etiology of such impairments and thus lack specificity. This presents particular challenges for screening and detection of conditions such as mild traumatic brain injury, which share a common symptom profile with fatigue due to sleep loss, including cognitive performance decrements (e.g., degraded attention, reaction time/RT, working memory, and executive system function) and changes in mood (e.g., irritability) (20). Additionally, implementation of these measures in field settings can be cumbersome and require trained examiners or clinicians to administer and interpret results. These limitations and the need for field-expedient, user-friendly tools to assess performance and readiness in service members from diverse occupational backgrounds, including flight crews, have led to a growing interest in novel metrics for assessment of degraded cognitive performance.

Physiology-based performance measures have drawn increasing interest as both independent and/or adjunct indicators of cognitive status. One such measure is a recently developed continuous predictive visual tracking task, designed to assess a construct of attention known as predictive timing (19). Unlike traditional attention assessment tools, this test specifically examines the dynamic interaction, i.e., synchronization, between the stimulus and action. Early work by Brezinova and Kendell (3) noted that visual tracking behavior in healthy subjects can be disturbed by fatigue. Humans use a combination of saccadic (quick repositioning) and smooth pursuit (continuous) eye movements to visually stabilize a moving object of interest on the fovea. Among its many functions, attention subserves the selection of visual information for processing (25) and, during visual tracking, these eye movements together reflect an overt expression of attention. Maintenance of visual tracking requires dynamic prediction of target velocity and trajectory, spatial working memory, and use of visual feedback to continuously adjust gaze position for accuracy (16). Numerous studies demonstrate that visual tracking is highly dependent on attention (2,16). Given that continuous and dynamic stabilization of the image of a moving object requires attention, quantification of visual tracking performance should provide a measure of attention system functioning.

Fatigue-related attention decrements represent a serious risk to human health and performance. The present study sought to characterize fatigue-related attention decrements in Army personnel within the first 26 h of sleep deprivation using a circular visual tracking paradigm. These results are then compared with attention performance as measured by the Attention Network Test (ANT) (7), a computer-based assessment specifically designed to delineate the efficiency of the alerting, orienting, and conflict components of attention.

METHODS

The present study, using a prospective, repeat measurement design, was conducted at an active duty military facility located in New England as part of a clinical research award to the Brain Trauma Foundation, New York, NY.

Subjects

The protocol was reviewed and approved by the local Army Institutional Review Board. Written informed consent was obtained from all subjects prior to data collection. Subjects were U.S. Army soldiers (68 men, 19 women; mean age 21.8 ± 3.7 yr, range 18-33 yr), representing diverse military occupational specialties (including infantry, mechanics, logistics and supply, mortuary assistants, and communications specialists) who were recruited from an active duty military facility in New England via scheduled, in-person briefings. Selection criteria for participation excluded individuals with prior history of traumatic brain injury/concussion with loss of consciousness, substance abuse, known neurologic disorders, and known psychiatric conditions (including attention deficit disorder). Participation required normal (or corrected to normal) vision and was limited to men and women, 18 to 50 yr of age, who had completed at least 12 yr of education and were able to abstain from caffeine use for at least 26 h.

After consent procedures were completed, prospective subjects underwent a structured screening interview conducted by a member of the research staff. This screening included the assessment for symptoms of attention deficit disorder (Conners Adult ADHD Rating Scale – Self-Report: Short Version; CAARS-S:S; Pearson, San Antonio, TX), posttraumatic stress disorder [Post Traumatic Stress Disorder (PTSD) Checklist – Civilian Version; PCL-C; National Center for PTSD, U.S. Department of Veterans Affairs], depression (Center for Epidemiologic Studies Depression Scale; CES-D) (26), and mild brain injury/concussion (Brain Injury Screening Questionnaire; BISQ) (11). Individuals were excluded from participation if they screened positive for ADD/ADHD symptomatology (t-score > 70 on the CAARS-S:S, or self-report of prior ADD/ADHD diagnosis) or brain injury (positive or "possible" brain injury rating on BISQ). Participant scores on the PCL-C and CES-D were included in subsequent analyses as covariates, if indicated.

Materials

Predictive visual tracking: A full description of the visual tracking protocol and analyses was reported by Maruta et al. (19) and is briefly summarized here. The visual

tracking protocol was carried out using a commercially available infrared visual-tracking system (EyeLink CL, SR Research, Ontario, Canada). Visual acuity was verified prior to testing using a Snellen chart. Subjects were seated comfortably with their heads stabilized using a head/chin rest during testing.

The semiautomated test sequence lasted approximately 5 min. During each test sequence, subjects received standardized instructions for test completion, calibration, and practice through both audio and visual formats. The test stimulus was a small target on a computer screen that moved along a circular trajectory of a 10° radius in visual angle six times at 0.4 Hz, and the participant was instructed to follow the target movement. Eye movements were recorded during two identical test runs.

Eye movement data were analyzed using a custom Matlab program (The MathWorks, Natick, MA). In the present study, primary visual tracking outcomes of interest were variability of gaze error along directions perpendicular and parallel to the target trajectory and mean phase error (MPE). Gaze error variability was measured with the SD of radial and tangential errors (SDRE and SDTE, respectively). These parameters were chosen as the primary outcomes of interest because precision and accuracy of continuous and dynamic predictive visual tracking relies upon one's ability to accurately predict where a target will appear (spatial prediction) and when it will appear (temporal prediction). Sleep loss/restriction has been shown to increase variability in performance across numerous tasks, including those assessing reaction time (simple and choice/decision RT), computational skills, sustained attention, and response inhibition (9,14,27). MPE is a measure of the overall temporal accuracy of visual tracking and is calculated as the average angular difference between the gaze and the target relative to the origin of the circular target trajectory (negative phase error = gaze trailing target or phase lag). SDRE and SDTE provide a measure of spatial and temporal precision of the gaze with respect to the moving target. Together, these measures provide an indication of gaze-target synchronization sensitive to lapses in attention (19,20).

Attention Network Test: The ANT (7) is a computer-based assessment of attention using RT measures and various cue and stimulus combinations. Subjects are asked to indicate the direction in which a central arrow is pointing. In some trials, the central arrow is presented alone and, in others, it is flanked by two arrows to either side that point in the same (congruent) or opposite (incongruent) directions. Cues providing temporal and spatial information pertaining to the target may also be presented.

In this study, the ANT variables of interest were: alerting effect (median RT of no-cue trials minus median RT of double cue trials); orienting effect (median RT of central cue trials minus median RT of spatial cue trials); executive control/conflict effect (EC/C; median RT of all incongruent flanker trials minus median RT of all congruent flanker trials); mean RT (average of raw response times for accurate responses across cue conditions); and accuracy (averaged across cue conditions). In the case of the alerting and orienting effects, a larger value may be inferred as either the ability to reduce the response time by taking advantage of cues or dependence on the cue presence to make a quick response. In the case of the EC/C effect, a larger value is inferred as a less efficient ability to resolve conflicting information.

Sleep questionnaire: At the start of the 26-h sleep deprivation period, subjects were asked to complete a 12-item questionnaire assessing their current level of wakefulness, amount of sleep achieved the preceding night, quality of sleep achieved, and use of sleep aids (e.g., prescription or over-the-counter medications or homeopathic supplements).

Procedure

The study measures were taken at three time points: 06:00-09:00 at the start of the 26-h sleep deprivation period (T1), 02:00-04:00 (T2, approximately 20 h awake), and 06:00-09:00 (T3, approximately 24-26 h awake). T2 represents a nadir in the circadian phase, while T3 represents the maximum cumulative period without sleep. Other tasks, including dynamic visual acuity testing and other neurocognitive measures, were carried out during the 26-h study period as part of a larger ongoing study of the effects of fatigue on physiologic and neurobehavioral performance in military service members; their results are, or will be, reported elsewhere (28).

A summary of activities throughout the 26-h sleep deprivation period is provided in **Table I**. Upon arrival for initial (T1) testing, subjects were briefed about study procedures and were allowed time to ask questions. Subjects then completed the testing protocol in the following order: sleep questionnaire, visual tracking protocol, brief break (5-10 min), ANT, and other measures (see below). The total time of T1 testing was 120-180 min. This test protocol, with the exception of the sleep

TABLE I. TIMELINE OF ACTIVITIES DURING 26 H OF SLEEP DEPRIVATION.

Time	Activity
06:00–09:00	Study briefing/instructions Initial testing (T1 – sleep questionnaire, eye tracking, ANT, other cognitive measures)
09:00–09:30	Breakfast
09:30–12:00	Military duties (trainings/briefings) Light physical activity (e.g., use of gym, playing video games, working on a computer)
12:00–13:00	Lunch
13:00–16:00	Military duties (trainings/briefings) Light physical activity (e.g., use of gym, playing video games, working on a computer)
16:00–17:00	Dinner
17:00–02:00	Light physical activity/low-impact recreation (e.g., use of gym, playing video games, working on a computer)
02:00–04:00	Testing (T2 – eye tracking, ANT, other cognitive measures)
04:00–06:00	Light physical activity/low-impact recreation (e.g., playing video games, working on a computer)
06:00–09:00	Testing (T3 – eye tracking, ANT, other cognitive measures)
09:00	24-h recovery

questionnaire, was repeated at T2 and T3. No subject had more than one previous exposure to the visual tracking paradigm or the ANT prior to T1. Throughout the remainder of the sleep deprivation period, subjects were encouraged to continue with normal daily activities, including normal military duties, trainings and briefings, and low-impact recreation, according to individual routine. Meals were taken as per usual schedule and a variety of nutritious snacks and beverages were provided; caffeine containing products were not permitted throughout the study period. One or more members of the research team accompanied subjects throughout the study period to ensure wakefulness, safety, and compliance to study procedures. Following completion of T3 testing, subjects were escorted to their barracks where they were allowed to recover for 24 h before resuming normal duties.

Statistical Analysis

Data analyses were completed using SPSS 19.0 (SPSS Inc., 2010, Chicago, IL). Descriptive analyses were initially conducted to assess sample characteristics and distribution of scores across measures. Outliers, identified as scores falling more than 3 SDs above or below the mean, were truncated to the 3-SD level. Distributions of scores for each measure were examined for skewness and kurtosis.

The relative impact of age, education, ethnicity, and gender on study outcome measures were examined using analysis of variance. A repeated measures analysis of variance (ANOVA) using Type III sums of squares was used to assess changes in visual tracking and ANT outcomes across the 26-h sleep deprivation period. Post hoc comparisons across the three discrete testing points (T2-T1, T3-T2, and T3-T1) were then completed for those variables demonstrating significance on ANOVAs by calculating a *t*-statistic using Type III mean square error. The relationships between visual tracking measures and ANT outcomes were assessed via Spearman correlations. The alpha level was set at 0.05 and a Bonferroni adjustment was made to account for multiple comparisons when appropriate. Calculated *P*-values that were smaller than 10^{-4} are expressed as < 0.0001; otherwise exact *P*-values rounded to the third decimal place are provided.

RESULTS

A total of 97 subjects were enrolled in this study. Two subjects were withdrawn after screening positive for having a history of head injury with loss of consciousness (BISQ), two subjects were withdrawn due to illness unrelated to the study procedures, and six subjects withdrew due to changes in military duty requirements. None of the subjects screened positive for ADD/ADHD. A total of 87 subjects were included in the final sample. Subjects reported an average of 12.6 yr (SD = 1.2 yr) of formal education and 8.7 mo (SD = 2.7 mo) of active duty service in the Army, and identified their racial/ethnic background as 54% Caucasian ($N = 47$), 24.1% African American ($N = 21$), 17.2 Hispanic/Latino ($N = 15$), and 4.6% as "other" ($N = 4$). On average, they scored within normal limits compared to the general (nonclinical) population on the PCL-C (mean = 21.1, SD = 5.5) and CES-D (mean = 5.2, SD = 4.7).

Identifying and truncating statistical outliers at the 3-SD value limit impacted scores on 1.5% of the visual tracking parameters and 1.1% of the ANT measures at T1, 3.1% of the visual tracking parameters and 1.4% of the ANT measures at T2, and 2.3% of the visual tracking parameters and 1.4% of the ANT measures at T3. Attempts were made to reduce the skewness of score distributions on the study measures with a log transformation. However, analyses conducted using log transformed values produced similar outcomes to those conducted using the raw values. Thus, analyses in this report were conducted using raw values.

Subjects were medically screened and cleared for any conditions that would prohibit their participation in research prior to the start of this study. Although not specifically queried, none of the subjects reported a history of disordered sleeping. All subjects adhered to a similar work schedule, beginning with morning formation at 06:30 and ending at 16:30. Sleep-wake cycles were per individual preference. In the 24 h prior to the start of this study, subjects reported sleeping an average of 6.69 h (SD = 1.7; ranging from 3 to 12.25 h) and none reported use of medication or homeopathic aid to assist achieving sleep. When queried about caffeine intake in the 24 h prior to the start of testing procedures, the majority of subjects reported consuming no caffeinated beverages (71.3%), while 23% ($N = 20$) reported consuming 1-2 caffeine-containing beverages and only 5 (5.7%) reported drinking 3-4 caffeinated beverages. None of the subjects reported or were observed to experience adverse reaction to abstinence from caffeine (e.g., severe headache) during the 26-h study period. The majority of subjects (85%, $N = 74$) indicated feeling moderately to completely well-rested at the start of testing.

SDRE and SDTE visual tracking parameters demonstrated a significant degradation in performance over time [SDRE: $F(2, 172) = 25.22$, $P < 0.0001$, and SDTE: $F(2, 172) = 21.14$, $P < 0.0001$] (**Table II**, **Fig. 1**). Post hoc pairwise comparisons using a Bonferroni adjusted alpha level of 0.017 (0.05/3) examining changes between discrete time points (T2 vs. T1, T3 vs. T2, and T3 vs. T1) generally showed a significant and monotonic increase in gaze error variability (both radial and tangential) across the 26-h study period (Table II). The largest observed changes occurred between T3 and T1 for both SDRE (mean difference = 0.28°, $P < 0.0001$) and SDTE (mean difference = 0.36°, $P < 0.0001$). A measure of predictive temporal gaze accuracy (MPE) did not change significantly from a rested state to 26 h without sleep.

Out of the five ANT indices, all except orienting effect showed an overall significant change in performance across the sleep deprivation period using an adjusted alpha of 0.01 (0.05/5) (**Table III**). Accuracy decreased [$F(2, 172) = 53.59$, $P < 0.0001$] and overall mean RT increased across the 26-h study period [$F(2, 172) = 40.39$,

TABLE II. VISUAL TRACKING SUMMARY STATISTICS.

	SDRE	SDTE	MPE
	(° in visual angle)		(° in phase angle)
Mean (SD)			
T1	0.59 (0.25)	0.80 (0.45)	-0.84 (1.87)
T2	0.68 (0.33)	0.98 (0.60)	-0.35 (2.24)
T3	0.87 (0.42)	1.17 (0.68)	-0.55 (2.74)
Overall model			
F (*P*)	25.22 (< 0.0001)*	21.14 (< 0.0001)*	2.53 (0.083)
Mean Square Error	0.070	0.135	2.05
d.f.	2, 172	2, 172	2, 172
Mean Difference (*t*, *P*)			
T2-T1	0.10 (2.41, 0.017)	0.17 (3.10, 0.002)*	-
T3-T2	0.18 (4.58, < 0.0001)*	0.19 (3.40, 0.001)*	-
T3-T1	0.28 (6.99, < 0.0001)*	0.36 (6.50, < 0.0001)*	-

Note: Overall model was examined using repeated measures ANOVA using Type III sums of squares.
*Statistically significant.
SDRE = standard deviation of radial error; SDTE = standard deviation of tangential error; MPE = mean phase error.
T1 testing occurred between the hours of 06:00-09:00; T2 testing occurred between the hours of 02:00-04:00 (approximately 20-22 h without sleep); T3 testing occurred between the hours of 06:00-09:00 (approximately 24-26 h without sleep).

$P < 0.0001$]. Pairwise comparisons involving three comparisons (T2-T1, T3-T2, T3-T1) and using an adjusted alpha of 0.017 (0.05/3) indicated that average response times (mean RT T3-T1 mean difference = 24.31 ms, $P < 0.0001$) and both the alerting and EC/C effects generally increased across the sleep deprivation period while response accuracy (ACC T3-T1 mean difference = −11.02%, $P < 0.0001$) declined significantly with each measurement over this time period.

Correlations (Spearman) between the visual tracking and ANT measures were used to provide a measure of interrelationship among different constructs of attention. Of the 15 pairs of visual tracking and ANT parameters, none of the baseline (T1) measurements showed significant correlations using an adjusted alpha of 0.0033 (0.05/15).

Concurrent validation of the visual tracking paradigm as a measure of attention was examined using correlations among changes in visual tracking and ANT indices across the sleep deprivation period (T3-T1). The eight indices that showed sleep deprivation-related changes were chosen for comparisons. Using an adjusted alpha of 0.006 (0.05/8), a significant correlation was observed between SDRE of visual tracking and ANT ACC (r = 0.301, $P = 0.005$), showing a small interdependence between decreases in gaze stability and response accuracy.

DISCUSSION

Continuous gaze-target synchronization during visual tracking is dependent upon attention (2,16,19). In this study, we examined the relationships among dynamic visuo-motor synchronization, other measures of attention, and acute total sleep deprivation of 26 h. Consistent with prior work indicating that decrements in vigilance cause increased variability (9,14,27), we found that sleep deprivation produced a significant decrease in the precision of gaze stabilization (SDRE, SDTE) during a predictive visual tracking task. This finding is also consistent with degradation of gaze positional control during periods of drowsiness (29). On the other hand,

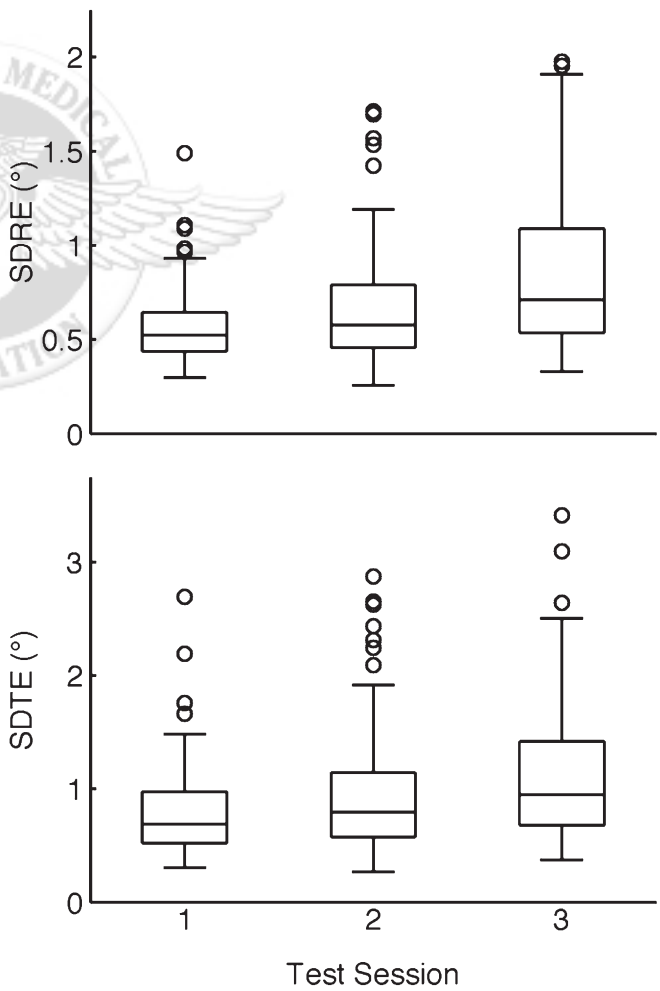

Fig. 1. SD of radial and tangential error across sleep deprivation period. SDRE = standard deviation of radial error. SDTE = standard deviation of tangential error. SDRE and SDTE are measured in degrees of visual angle.

TABLE III. ANT SUMMARY STATISTICS.

	Alerting (ms)	Orienting (ms)	EC/C (ms)	Mean RT (ms)	ACC (%)
Mean (SD)					
T1	37.1 (27.3)	40.5 (22.9)	111.2 (41.8)	556.9 (67.9)	98.7 (1.4)
T2	48.3 (28.5)	46.8 (31.3)	116.6 (40.2)	574.2 (73.2)	96.3 (5.1)
T3	61.4 (48.3)	51.5 (32.4)	148.2 (62.7)	609.6 (78.6)	87.6 (13.7)
Overall model					
F (*P*)	13.04 (< 0.0001)*	3.71 (0.033)	34.46 (< 0.0001)*	40.39 (< 0.0001)*	53.59 (< 0.0001)*
Mean Square Error	987.2	714.5	1005.3	1552.7	54.71
d.f.	2, 172	2, 172	2, 172	2, 172	2, 172
Mean Difference (*t*, *P*)					
T2-T1	11.21 (2.35, 0.020)*	-	5.43 (1.13, 0.260)	17.26 (2.89, 0.004)*	−2.36 (−2.11, 0.037)
T3-T2	13.09 (2.75, 0.007)*	-	31.53 (6.51, < 0.0001)*	35.41 (5.93, < 0.0001)*	−8.66 (−7.73, < 0.0001)*
T3-T1	24.31 (5.10, < 0.0001)*	-	36.96 (7.69, < 0.0001)*	52.67 (8.82, < 0.0001)*	−11.03 (−9.83, < 0.0001)*

Note: Overall model was examined using repeated measures ANOVA using Type III sums of squares.
*Statistically significant.
EC/C = executive control/conflict; Mean RT = mean reaction time for correct response; ACC = accuracy.

the overall temporal relationship between the gaze and target (MPE) was not significantly impacted, also consistent with previous work (6).

We used the ANT to provide an additional measure of the attention construct. The weak correlations to visual tracking metrics at baseline suggest that the two tests measure largely separate but interacting attention constructs. As the period of sleep loss increased, subjects demonstrated longer response times and decreased accuracy on the ANT. A significant increase in the EC/C effect indicated decreased efficiency for resolving conflicting information with an increasing sleep deficit. This change was directionally opposite of that noted by Ishigami and Klein (12), who reported a reduced EC/C effect with as many as 10 repeated administrations of the ANT, thus demonstrating learning effects that can be expected under normal conditions. In contrast, practice effects are negligible for the visual tracking test (19). We speculate that the effect of fatigue due to sleep loss either obscured or eliminated any effects practice may have had on a participant's performance. These findings replicate, at least in part, those reported by Martella et al. (18) and Roca et al. (27). However, in contrast to these previous studies, we found a significant increase in the alerting effect as well. Consistent with prior studies (4,32), the observed increased RT facilitation due to a warning cue (enhanced alerting effect) most likely reflects an increase in overall response latencies due to sleep loss, rather than an increase in the participant's ability to take advantage of an alerting cue.

Correlations between the indices of the visual tracking test and ANT were weak, suggesting that the attention constructs assessed with these tests were largely independent. However, changes in the ANT accuracy index were correlated with changes in gaze stability over the sleep deprivation period, lending further support to the premise that predictive visual tracking reflects the overall integrity of the attention system.

It should be noted that subjects in this study were predominantly young, Caucasian men in excellent physical condition and in the early stages of their Army career. None of our subjects had a history of deployment or other combat-related activity. As a result, generalizing our current findings to both the broader population of military service members and civilians, including those within the aviation community, should be made with caution. The subtle nature of the findings reported here may be a reflection of the relatively healthy and robust nature of the present sample. In addition, the possible impact of such factors as caffeine withdrawal and individual sleep-wake patterns on the observed pattern of results cannot be fully determined within the context of the current study design.

Previous work has shown that impaired predictive timing can produce poor visual tracking using the same highly predictable circular visual tracking paradigm as used in the present investigation (20). In these studies, physical injury to brain regions supporting attention processes impaired visual tracking performance. The current study provides further evidence linking impairments in attentional processes, in the present case due to an acute, reversible stressor (sleep deprivation), to dynamic visuo-motor synchronization performance. These findings support the utility of this highly predictable visual tracking paradigm as an accurate and efficient measure of fatigue in healthy individuals. The implication that a simple oculomotor assessment may be used as a fitness-for-duty test is relevant to a range of fields, including military, aviation, and aeromedicine, where fatigue due to sustained operations and variations in operational pacing is a common cause for accidents and related injuries or fatalities. Further work is needed to validate such application.

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